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EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,319	SCHENK, DALE B.	
	Examiner	Art Unit	
	Sharon L. Turner	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12-15-05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *83 and 101-163* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-58,61,63-66,71-79,81,85,86,92-94,97,99,164-191,194-205 and 207-209* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *56-58, 61, 63-66, 71-79, 81, 83, 85-86, 92-94, 97, 99, 101-191, 194-205, 207-209* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12-15-05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 56-58,61,63-66,71-79,81,83,85,86,92-94,97,99,101-191,194-205 and 207-209.

Response to Amendment

1. The Examiner of U.S. Patent Application No. 09/724,319 has changed. In order to expedite the correlation of papers with the application, please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1649.

2. The amendment filed on 12-15-05 has been entered into the record and has been fully considered.

3. Claims 56-58, 61, 63-66, 71-79, 81, 83, 85-86, 92-94, 97, 99, 101-191, 194-205, 207-209 are pending. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, 207-209 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn.

6. Claims 83, 101-163 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4-5-04.

7. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, 207-209 are under examination.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, 207-209 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-44, 134-135, 138-139, 142-145, 146, 148 and 154-157 of Application No. 09/979701. As previously noted the claims overlap in antibody composition and administration of antibody for treatment and or prevention as encompassed by instant language directed to delaying onset or reducing risk.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request that the double patenting rejection be held in abeyance until such time that a notice of allowance is issued. Applicants do concede that certain issues are in conflict between the two applications.

Rejection is maintained as set forth in MPEP 804, the "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Claim Rejections - 35 USC § 112,

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, 207-209 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's have amended the claims to recite human antibody 266 that specifically binds to epitope of residues 13-28 of Aβ. The specification and prior art recognize mab 266 but the antibody is a mouse monoclonal. The specification does not disclose a human mab266, such was not deposited nor does

the specification evidence that any such antibody was made or was in the possession of Applicants. Accordingly, the recitation lacks adequate written description support and constitutes new matter absent evidence of support.

12. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 183-191, 194-205, 207-209 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing amyloid plaquen burden, does not reasonably provide enablement for treating, reducing risk or delaying onset where treating is synonymous to cure and/or prevention of Alzheimer's disease in a patient and the treatment is not so linked to the administration noted to provide for such effects constituting specific administration protocols. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner notes Applicant's amendments to recite "treating a patient having Alzheimer's disease" to human antibody, to pharmaceutical carriers and compositions and to reducing risk or delaying onset.

However, the specification is still insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims.

The specification does not define treatment and only provide guidance to a measure of reducing risk or delaying onset for example as noted at p. 27. The

description is akin to previously recited "therapeuticall treating," and inclusive of cure or at least alleviating. As previously noted, Stedman's Medical Dictionary defines therapeutic as follows:

> Therapeutic: Relating to therapeutics or to the treatment, remediating, or curing of a disorder or disease. [G. therapeutikos]

Thus, even the recitation of "treating" and recitations of reducing risk or delaying onset appear to be delineated via inclusion of curing the disease, which is not enabled by the instant disclosure. Moreover the choice of any alleviation where multiple symptoms and effects are present fail to distinguish the scope of the recitation to any particular effect. The Examiner does note that certain specific treatments were noted to provide for reduced amyloid plaque burden. Support is therefore acknowledged for this recitation where the data are commensurate with the recitation but not to inclusion of curing or effects noted in diseased patients that are not fairly represented via the animal model data. In the instant case, the model system used in the instant Specification is not recognized as providing the teachings that are predictive of the results which would be expected for the full scope of the claims. As noted above, the claims are inclusive of "curing." The state of the art is such that there is currently no known cure for Alzheimer's disease (Ankarcrona and Winblad, Int Journal of Geriatric Psychiatry, 2005, 20:101-105; Souder and Beck Nurs Clin North Am., Sep 2004, 39(3):545-59), and those skilled in the art recognize that such technology is currently beyond scope.

Furthermore, as note in the previous Office Action (4/26/2004, pg 6), the specification teaches that the administration of particular anti-Aβ antibodies is able to reduce β-amyloid levels within the brains of mice, which are transgenic for PDAPP and

exhibit Alzheimer's type over production and build up of β-amyloid within the brain. Thus, while the specification demonstrates a level of protection using anti-Aβ antibodies for passive immunization in the PDAPP mice, "curing" and ""prevention" were not achieved. The specification also discloses "patient" includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment. The specification, as noted above, teaches reduced β-amyloid levels within the brains of mice. The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed. The specification fails to provide any guidance for successfully "therapeutically treating" or ""prophylactically treating" human patients with Alzheimer's disease, and since resolution of the various complications in regards to treating Alzheimer's disease with an antibody is not complete, one of skill in the art would be unable to practice the invention without engaging in undue trial and error experimentation. The specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed methods. Additionally, a person skilled in the art would recognize that predicting the efficacy of anti-Aβ in humans in an Alzheimer's disease model as highly problematic (see MPEP §2164.03). Thus, although the specification prophetically considers and discloses general methodologies of using the claimed methods, such a disclosure would not be considered enabling since the state of the treatment of Alzheimer's diseases is highly unpredictable.

While the use of anti-Aβ antibodies wherein said antibodies are specific for an epitope comprising residues 13-28 of Aβ is feasible for treating Alzheimer's disease, Spooner *et al.* (13 December 2002, *Vaccine* 21(3-4): 290-297) teaches that the route of

administration, the regiment of administration, and the genetic background of the mouse used affects the production of anti-Aβ antibodies in response to Aβ immunization (Table 1 and 2). It is also noted that although no deleterious effects were observed, this too could be dependent upon genetic factors of the animal receiving the immunization (pp. 296). Thus, uncertainty is found by use of Aβ as an immunogen in regards to possible autoimmune reactions, general deleterious side effects, and variability in the production of anti-Aβ antibodies. Furthermore the Specification teaches that the 266 antibody binds to monomeric but not aggregated Aβ (pp. 70 lines 19-20).

Walker *et al.* (July 1994, *Journal of Neuropathology and Experimental Neurology* 53(4): 377-383 (**IDS#169**) teaches the administration of a monoclonal anti-β-amyloid antibody (10D5) into the cerebrospinal fluid of aged monkeys (pp. 377). Following injection, the monkeys were sacrificed and their brains examined to confirm that the antibodies injected labeled Aβ plaques (Figures 1-5).

Also concerning passive immunization, Goldsby *et al.* (2002) *Kuby Immunology* 4th Ed. Chapter 18 "Vaccines" (pp. 449-465) teaches that passive immunization does not allow for the formation of immunological memory requiring continued dosages if the desired immunity is to be maintained. Also the issue of the antigenicity of the antibody administered must be taken into consideration because it can trigger and unwanted and possibly harmful immune response especially mouse antibodies administered to humans (pp. 451). Therefore, inadequate guidance is presented in the Specification to overcome these obstacles in practicing the invention to the full scope as claimed.

The specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from treatment and risk assessment of Alzheimer's disease in animals to humans as exemplified in the references herein. Thus, for the aforementioned reasons therapeutic or prophylactic treatment of Alzheimer's disease in humans does not appear to be commensurate in scope with the claims {see Sipe (1992) *Annu. Rev. Biochem.* 61: 947-975}.

Applicants argue in the 12-15-05 response that the amendments obviate rejection on these grounds, that the teachings of the specification are sufficient to provide enablement and that the cited references to not contraindicate.

Applicants arguments have been fully considered but are not persuasive as the preamble recitations are inclusive of treatments that are currently beyond scope. A mere showing of reduced plaque burden does not speak to the elements encompassed in cluding complete resolution and/or prevention of plaque formation or any effect noted in disease such as loss of cognitive function, reduced learning and memory. Rejection therefore is maintained as the teachings of the specification are not of commensurate scope with the claims.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, and 207-209 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,593,846 (14 January 1997) Schenk *et al.*, further in view of US 5,530,101 (25 June 1996) Queen *et al.*

US Patent 5,593,846 teaches an antibody whose epitope lies within residues 13-28 of Aβ and is known as 266, thus meeting the limitations of claims 97 and 99 (See Col. 4, lines 60-67; Col. 5, lines 1-5 and 28-35; Col. 13, lines 35-40; Col. 14, lines 13-28; and claim 7). The claims recite a pharmaceutical composition of an antibody which specifically binds to an epiptope within residues 13-28 of Aβ and wherein said antibody is designated as "266". US 5,593,846 teaches an antibody, and antibody fragments (pg 9), including monoclonal and polyclonal and fragments (Fab, Fv, etc.), whose epitope lies within residues 13-28 of Aβ and is known as 266. The US Patent further discloses fragments and "recombinantly produced antibodies (immunoglobulins) and variations thereof" (pg 8) that are well described in the patent and scientific literature including Harlow and Lane, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory), 1988. The reference teaches fusion to a bacterial protein (pg 17).

The US patent is silent to chimeric or humanized antibodies as recited in the claims. However, the '586 patent makes reference to "**recombinantly produced antibodies**" and thus is deemed to be inclusively directed to recombinantly produced antibodies which are humanized antibodies and/or chimeric antibodies (pg 8). The '586 patent does not elaborate on such procedures, but instead refers to common knowledge of the artisan as further referenced with direction to the reference incorporated in the

patent by Harlow and Lane (1988), methods of producing various antibodies including chimeric and humanized. Such is further supplemented here by Queen, US 5,530,101. The '586 reference contemplates pharmaceutical compositions incorporating a therapeutic or prophylactic amount of at least one compound and a pharmaceutically acceptable carrier. The pharmaceutically acceptable carrier can be any compatible, non-toxic substance suitable to deliver the compounds to an intended host, for example sterile water, alcohol, fats, waxes, and inert solids; pharmaceutically acceptable adjuvants, buffering agents, dispersing agents; and active agents (pg 11-12), which are all well described in the medical and scientific literature. Particularly, the reference teaches the antibody diluent consisted of Trizma base (see ELISA Assay protocol), and the antibody in phosphate-buffered saline (see antibody preparation). Thus, the reference meets the limitations of claims 165-169 and 172-182. The reference also contemplates the pharmaceutical compositions is suitable for systemic administration to the host, including both parenteral, topical, and oral administration and that the pharmaceutical compositions may be administered parenterally, i.e. subcutaneously, intramuscularly, or intravenously (pg 11-12). The recitation in the claims, "pharmaceutical composition" is interpreted as an intended use and is not given patentable weight in this art rejection, and the composition of US 5,593,846 is not inconsistent with such a composition. Thus, the reference meets all the limitations in the claims. The composition is administered to a host susceptible to the disease, but not already suffering from such disease identified by genetic screening and clinical analysis (pg 12). The following excerpts are particularly noted.

Brief Summary Text (3):
The present invention relates generally to methods and compositions for detecting soluble .beta.-amyloid peptide (.beta.AP) in fluid samples. More particularly, the present invention relates to screening methods for the identification of inhibitors of .beta.AP production where .beta.AP is detected in vitro or in vivo and to diagnostic methods where .beta.AP is detected in patient samples.

Brief Summary Text (9):
Despite the progress which has been made in understanding the underlying mechanisms of AD and other .beta.AP-related diseases, there remains a need to develop methods and compositions for diagnosis and treatment of the disease(s). Treatment methods could advantageously be based on drugs which are capable of inhibiting the generation of .beta.AP in vivo. To identify such drugs, it would be desirable to provide screening assays for potential drugs which can inhibit .beta.AP generation in in vivo and in vitro models. It would be further desirable to provide methods and compositions for diagnosis of .beta.AP-related conditions, where the diagnosis is based on detection of .beta.AP in patient fluid samples. Specific assays for .beta.AP detection should be capable of detecting .beta.AP in fluid samples at very low concentrations as well as distinguishing between .beta.AP and other fragments of APP which may be present in the sample.

Brief Summary Text (18):
The present invention provides methods and compositions useful for the identification of .beta.-amyloid peptide (.beta.AP) production inhibitors as well as for the diagnosis and monitoring of .beta.AP-related conditions in patients, where the methods and compositions rely on the specific detection of soluble .beta.AP and/or .beta.AP fragments in fluid samples. For the identification of .beta.AP production inhibitors, a test compound is introduced to an in vitro or in vivo .beta.AP generation model, and the effect of the test compound on the amount of soluble .beta.AP or .beta.AP fragment generated by the model is observed. Particularly useful as an in vitro model are cell lines which express APP variants which overproduce .beta.AP. Test substances which affect the production of .beta.AP and/or .beta.AP fragments, usually by reducing the amount produced, are considered to be likely candidates for further testing for use as therapeutic drugs in the treatment of .beta.AP-related conditions, particularly Alzheimer's Disease. For the diagnosis and monitoring of .beta.AP-related conditions, the amount of soluble .beta.AP and/or .beta.AP fragments in a patient sample, such as blood, cerebrospinal fluid (CSF), urine, or peritoneal fluid, is measured and compared with a predetermined control value, such as a normal value (in the case of diagnosis) or a prior patient value (in the case of monitoring).

Detailed Description Text (29):
The present invention further comprises pharmaceutical compositions incorporating a compound selected by the above-described method and including a pharmaceutically acceptable carrier. Such pharmaceutical compositions should contain a therapeutic or prophylactic amount of at least one compound identified by the method of the present invention. The pharmaceutically acceptable carrier can be any compatible, non-toxic substance suitable to deliver the compounds to an intended host. Sterile water, alcohol, fats, waxes, and inert solids may be used as the carrier. Pharmaceutically acceptable adjuvants, buffering agents, dispersing agents, and the like may also be incorporated into the pharmaceutical compositions. Preparation of pharmaceutical conditions incorporating active agents is well described in the medical and scientific literature. See, for example, Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa., 16th Ed., 1982, the disclosure of which is incorporated herein by reference.

Detailed Description Text (30):
The pharmaceutical compositions just described are suitable for systemic administration to the host, including both parenteral, topical, and oral administration. The pharmaceutical compositions may be administered parenterally, i.e. subcutaneously, intramuscularly, or intravenously. Thus, the present invention provides compositions for administration to a host, where the compositions comprise a pharmaceutically acceptable solution of the identified compound in an acceptable carrier, as described

above.

Detailed Description Text (31):
Frequently, it will be desirable or necessary to introduce the pharmaceutical compositions directly or indirectly to the brain. Direct techniques usually involve placement of a drug delivery catheter into the host's ventricular system to bypass the blood-brain barrier. Indirect techniques, which are generally preferred, involve formulating the compositions to provide for drug latentiation by the conversion of hydrophilic drugs into lipid-soluble drugs. Latentiation is generally achieved through blocking of the hydroxyl, carboxyl, and primary amine groups present on the drug to render the drug more lipid-soluble and amenable to transportation across the blood-brain barrier. Alternatively, the delivery of hydrophilic drugs can be enhanced by intra-arterial infusion of hypertonic solutions which can transiently open the blood-brain barrier.

Detailed Description Text (32):
The concentration of the compound in the pharmaceutical carrier may vary widely, i.e. from less than about 0.1% by weight of the pharmaceutical composition to about 20% by weight, or greater. Typical pharmaceutical composition for intramuscular injection would be made up to contain, for example, one to four ml of sterile buffered water and one .mu.g to one mg of the compound identified by the method of the present invention. The typical composition for intravenous infusion could be made up to contain 100 to 500 ml of sterile Ringer's solution and about 1 to 100 mg of the compound.

Detailed Description Text (33):
The pharmaceutical compositions of the present invention can be administered for prophylactic and/or therapeutic treatment of diseases related to the deposition of .beta.AP, such as Alzheimer's disease, Down's syndrome, and advanced aging of the brain. In therapeutic applications, the pharmaceutical compositions are administered to a host already suffering from the disease. The pharmaceutical compositions will be administered in an amount sufficient to inhibit further deposition of .beta.AP plaque. An amount adequate to accomplish this is defined as a "therapeutically effective dose." Such effective dose will depend on the extent of the disease, the size of the host, and the like, but will generally range from about 0.01 .mu.g to 10 mg of the compound per kilogram of body weight of the host, with dosages of 0.1 .mu.g to 1 mg/kg being more commonly employed.

Detailed Description Text (34):
For prophylactic applications, the pharmaceutical compositions of the present invention are administered to a host susceptible to the .beta.AP-related disease, but not already suffering from such disease. Such hosts may be identified by genetic screening and clinical analysis, as described in the medical literature (e.g. Goate (1991) Nature 349:704-706). The pharmaceutical compositions will be able to inhibit or prevent deposition of the .beta.AP plaque at a symptomatically early stage, preferably preventing even the initial stages of the .beta.-amyloid disease. The amount of the compound required for such prophylactic treatment, referred to as a prophylactically-effective dosage, is generally the same as described above for therapeutic treatment.

The reference, US 5,593,846 does not recite a “chimeric or humanized” antibody.

However, it would have been obvious to the person of ordinary skill in the art at the same time the invention was made to modify the teachings of Schenk *et al.* and to utilize recombinantly produced humanized and/or chimeric antibodies.

As in Queen, chimeric antibodies are successful in overcoming the limitations of monoclonal antibodies and humanized antibodies are important because they bind to the same antigen as the original antibodies, but are less immunogenic when injected into humans (Queen, US 5,530,101, see Background of the Invention, pg 1-2). The person of ordinary skill in the art would have been motivated to make the modifications because humanized and chimeric antibodies, which have the same or similar binding specificity and affinity as the nonhuman antibody that provides the starting material for its construction are useful in treating diseases in humans whereas antibodies, such as monoclonal antibodies especially of non-compatible host structure are hyper-immunogenic when injected into humans. The person of ordinary skill in the art would have reasonably expected success because methods of producing chimeric or humanized antibodies are well described in the art.

In the 12-15-05 response Applicants argue that the claims are not obvious in view of Queen as the patent does not rectify a lack of teachings with respect to methods of treatment, delay or reduction in risk. Applicants argue no motivation for therapeutic administration from the assays utilized for detection.

Applicants arguments have been fully considered but are not persuasive. As set forth in the rejection of record and elaborated herein, the '846 patent is on point for therapeutic benefit and accordingly the administration of the antibody with correct epitope is the same. The only difference is that the 266 antibody of the patent is a mouse monoclonal. Yet both the '846 patent and Queen motivate to administration of humanized or chimeric antibodies for reduced hyperimmunogenicity, particularly when

used for such therapeutic purposes. The '846 patent is on point to recombinantly produced antibodies. This is art accepted terminology for referral to chimeric or humanized antibodies as these are made via means of recombinant technology as opposed to clonal production from a naturally immunized cell although the '846 patent is silent to these specific procedures. Nevertheless, Queen evidences the art accepted procedures for making recombinant antibodies termed chimeric or humanized and motivate to use such for in vivo therapy. Thus, the cumulative reference teachings render the claimed invention obvious to the artisan.

Conclusion

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Thursday from 7:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at (571) 272-0867.

Sharon L. Turner, Ph.D.
April 30, 2006

SHARON TURNER, PH.D.
PRIMARY EXAMINER

4-30-06